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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/529,925	07/30/2000	ELIAS GEORGES	641050.90013	9902

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JEAN C BAKER
QUARLES & BRADY
411 EAST WISCONSIN AVENUE
SUITE 2550
MILWAUKEE, WI 53202-4497

EXAMINER	
ROBINSON, HOPE A	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 08/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/529,925	GEORGES ET AL.	
	Examiner	Art Unit	
	Hope A. Robinson	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6,7,15,17,18,20-27,30-33,36,37 and 39-45* is/are pending in the application.

4a) Of the above claim(s) *6,7,24-27,30,31 and 36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *15,17,18,20-23,32,33,37 and 39-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. Applicant's response to the Office Action mailed November 19, 2003 on May 21, 2004 is acknowledged.

Claim Disposition

2. Claims 1-5, 8-14, 16, 19, 28-29, 34-35, and 38 have been canceled. Claims 43-45 have been added. Claims 17, 20, 32, 39 and 41-42 have been amended. Claims 6-7, 15, 17-18, 20-27, 30-33, 36-37 and 39-45 are pending. Claims 15, 17-18, 20-23, 32-33, 37 and 39-45 are under examination.

3. The following grounds of rejection are or remain applicable:

Claim Objection

4. Claims 15, 20, 37 and 39 are objected to because of the following informalities:

For clarity claims 15, 20, 37 and 39 should be amended to remove the recitation of "Annexin's expression" and instead recite "the expression of Annexin". The dependent claims hereto are also included in this objection.

Claim 20 is objected to because the spelled out meaning of the acronym MDR should follow the first appearance of the acronym.

Claim Rejections - 35 U.S.C. § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 32-33 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Note that claim 32 (and dependent claim 33) are directed to methods with no method steps. As the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. Note that claim 32 which is directed to a method of conferring drug resistance to a cell only provides results, not method steps *per se*, such as an increase in protein expression. Without setting forth any steps involved in the process/method, results in an improper definition of a process and is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and

distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 17-18, 20-23, 32-33 and 39, 41-42 and 44-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 is indefinite for the recitation of "a nucleic acid molecule encoding an Annexin antisense molecule", as DNA encodes proteins not other DNAs. The dependent claim hereto is also included.

Claim 20 is indefinite for the recitation of: "a cell having been rendered multidrug resistance by an expression of Annexin", because 1) the phrase rendered multidrug resistance" is improper and should be "rendered multidrug resistant" (see also claim 39 for the same language); and 2) "by an expression of an Annexin" is improper and should be "by expression of Annexin" (see also claim 39 for the same language).

Claim 32 lacks antecedent basis for "confers MDR" as the claim is directed to a method of conferring drug resistance to a cell". In addition, claim 32 lacks antecedent basis for "said increased expression" as line two of the claim recites "increase in the expression". The dependent claim hereto is also included in this rejection.

Claims 32 and 39 remain indefinite because the mere recitation of the acronym MDR is not sufficient to convey what applicant intends the invention to be and for clarity all independent claim should recite the spelled out meaning of the acronym.

Claim 42 is indefinite for the recitation of "an nucleic acid molecule", instead of "a nucleic acid molecule".

Claim Rejections - 35 U.S.C. §103

The following is a quotation of 35 U.S.C. 103 (a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103 (a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103 (c) and potential 35 U.S.C. 102 (f) or (g) prior art under 35 U.S.C. 103 (a).

8. Claims 15, 20-21, 32-33, 37, 40, 43 and 44 are rejected under 35 U.S.C. 103(a) as obvious over Wang et al. (Biochemical and Biophysical Research Communications, vol. 236, pages 483-488, 1997) based on the disclosure which states that P-40 is Annexin I and that the invention relates to the identification of Annexins (I-XI, also referred to herein as P-40 and P-40 homologs (see page 4 of the specification).

Wang disclose a method comprising the binding of IMP96 to P-40 in MCF-7/Adr cells (see Figure 1 of the reference) and demonstrates that P-40 (Annexin I) confers resistance to Taxol and Adriamycin (see Table 1 and discussion on page 486 of the reference). Wang further discloses that the over expression of P-40 in paclitaxel or cis-platinum selected cell lines, in the absence of a detectable level of P-gp or MRP supports the notion that P-40 alone may confer resistance to cytotoxic drugs (claims 32-33, see page 486 of reference). Wang also disclose that P-40 could modulate an MDR phenotype indirectly, by stating that P-40 may be a component of the apoptosis signaling pathway (see claims 15 and 37). Moreover, Wang discloses that changes in the levels or functions of proteins involved in the signaling of apoptosis can confer an MDR phenotype on tumor cells (see page 487). Wang also disclose a method that identifies a protein that mediates drug resistance to anticancer drugs (claims 20-21). Wang further discloses a method that was used to isolate a monoclonal antibody (IPM96) which recognized a protein (P-40) co-expressed with P-glycoprotein in several resistant cell lines. Additionally, Wang discloses that over expression of P-40 (protein which is Annexin) in multidrug resistant cells may be important in the expression of the drug resistance phenotype (see pages 483-485).

The Wang reference identifies a compound (P-40) that affects Annexin-based MDR in a cell in the presence of a drug (Adriamycin and Taxol) and assessed the effect of said compound as claimed in the present application. Further, Wang discloses a method that utilizes an antibody to Annexin (claims 43-44) and a compound that modulates Annexin based MDR in a cell as the present application discloses that P-40 and Annexin are equivalent. Although Wang does not teach a direct correlation as recited in claim 20 for example, it would have been obvious to one of ordinary skill in the art to arrive at the claimed invention as a whole because Wang teaches that there is an

indirect correlation and that P-40 is important in the expression of drug resistance phenotype, thus provides a suggestion for a direct correlation. Furthermore, it is not apparent whether or not a method in which cell membrane integrity is compromised would or would not be considered to be "direct". Thus, the claimed invention was obvious to make and use at the time it was made and was *prima facie* obvious.

9. Applicant's arguments filed on May 21, 2004 have been fully considered but were not persuasive.

Regarding the rejections under 35 U.S.C. 112, second paragraph, applicant's comments are noted, however, some issues raised in the previous office action were not addressed, for example, claims 32 and 39 were not amended to recite the spelled out meaning of the acronym MDR, thus the rejections remain. In addition, new grounds of rejections have been instituted based on amendments made and for the reasons stated above.

Note also that a new ground of rejection has been instituted under 35 U.S.C. 101 for the reasons stated above.

With regard to the rejection under 35 U.S.C. 103, the comments on pages 8-9 are noted. Applicant argues that the "Wang reference is simply an incentive to pursue experiments". It is further stated that "although it may be said that from Wang's results it would be obvious to try to show that P-40 caused MDR -- this is not the test for determining obviousness". Applicant conclude that Wang's authors themselves did not come to the conclusion that P-40 caused MDR. Applicant's assertions are not completely accurate as the Wang reference disclose that:

1) " ... the over expression of P-40 in multidrug resistant cells have been previously determined and therefore could be important in the expression of the drug resistance phenotype" (see abstract);

2) "..the observed decrease of P-40 levels in a revertant cell line (H69/PR) derived from H69/AR, together with the above results, suggest a correlation between the P-40 expression and drug resistance in H69/AR cells" (see right column on page 486);

3) "[I]n conclusion, we show the over expression of a 40 kDa protein in MDR cells in the presence and absence of P-gp or MRP. Although further studies are required to demonstrate a direct role for P-40, if any, in drug metabolism and MDR; P-40 could modulate an MDR phenotype indirectly. For example, P-40 may be a component of the apoptosis signaling pathway. There is now growing evidence that changes in the levels or the functions of proteins involved in the signaling of apoptosis can confer an MDR phenotype on tumor cells" (see right column on page 487).

Note that Wang indicates further study is necessary for a direct role for P-40, however, discloses an indirect role for P-40 in modulating the MDR phenotype. Therefore, the suggestion made in the reference of record meets the requirement under 35 U.S.C. 103(a) (a mere teaching or suggestion). Thus, Applicant's arguments are not persuasive and the Wang reference remains relevant.

Conclusion

10. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday from 9:00 a.m. to 6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber, can be reached at (571) 272-0925.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hope A. Robinson, MS
Patent Examiner
5/6/04

Jon P. Weber, Ph.D.
Primary Examiner